

**LISTING OF CLAIMS**

1. (Currently amended) An isolated polynucleotide comprising:
  - a) a first nucleic acid sequence encoding a CD8  $\alpha$ -chain comprising a CD8  $\alpha$ -chain extracellular domain;
  - b) a second nucleic acid sequence encoding a therapeutic molecule of interest; and
  - c) separate transcription control elements ~~and~~ having associated translational control elements for directing separate expression of said first and said second nucleic acid sequences.
2. (Previously presented) The polynucleotide according to claim 1, wherein said CD8  $\alpha$ -chain comprises all or a functional portion of a human CD8  $\alpha$ -chain.
3. (Canceled)
4. (Previously presented) The polynucleotide according to claim 1 or 2, wherein said CD8  $\alpha$ -chain consists essentially of an extracellular domain of said CD8  $\alpha$ -chain and a transmembrane domain.
5. (Previously presented) The polynucleotide according to claim 4, wherein said transmembrane domain is a CD8  $\alpha$ -chain transmembrane domain.
6. (Previously presented) The polynucleotide according to claim 4, wherein said transmembrane domain is a synthetic transmembrane domain.

7. (Currently amended) The polynucleotide according to claim 1, wherein said therapeutic molecule of interest is selected from the group consisting of hemoglobin- $\beta$ , GATA-binding protein, d-aminoevalinate synthase, glucose-6-phosphate-dehydrogenase, Coagulation Factor VIII, Coagulation Factor XI, cystic fibrosis transmembrane conductance regulator, ornithine carbamoyl transferase,  $\alpha$ -L-iduronidase, iduronate-2-sulfatase,  $\beta$ -hexosidase  $\beta$ -glucosidase,  $\alpha$ -galactosidase, galactosylceramidase, acid  $\alpha$ -glucosidase, hexamidase A, phenylalanine hydroxylase, collagen type IV,  $\alpha 5$ , Bloom Syndrome Gene Product, and low density lipoprotein receptor.

8. (Previously presented) An expression vector comprising the polynucleotide according to claim 1 or to claim 7.

9. (Previously presented) The expression vector according to claim 8, wherein said vector is selected from the group consisting of a recombinant adenovirus, a recombinant retrovirus, a recombinant adeno-associated virus, and a recombinant herpes virus.

10. (Previously presented) The expression vector according to claim 9, wherein said vector is replication defective.

11. (Currently amended) An expression vector according to claim 8 for expression in a target cell, wherein ~~said expression of said CD8  $\alpha$ -chain by said target cell~~ is designed to inhibit[[s]] an immune response against vector-associated antigens, when expressed by said target cell.

12-17. (Canceled)

18. (Currently amended) An expression vector according to claim 8 for expression in a target cell, wherein ~~said expression of~~ said CD8  $\alpha$ -chain is designed to inhibit[[s]] an immune response against said expression vector, when expressed.

19. (Currently amended) An improved viral expression vector having reduced immunogenicity comprising a non-viral nucleic acid consisting essentially of a nucleic acid sequence encoding a CD8  $\alpha$ -chain comprising a CD8  $\alpha$ -chain extracellular domain and a nucleic acid encoding for a therapeutic molecule of interest, wherein said CD8  $\alpha$ -chain and said therapeutic molecule are separately expressed as a function of separate transcription control elements.

20. (Currently amended) An isolated polynucleotide comprising:

- a) a first nucleic acid sequence encoding a CD8  $\alpha$ -chain comprising a CD8  $\alpha$ -chain extracellular domain, wherein the CD8  $\alpha$ -chain is not a fusion protein;
- b) a second nucleic acid sequence encoding a therapeutic molecule of interest; and
- c) separate transcription control elements ~~and~~ having associated translational control elements for directing separate expression of said first and said second nucleic acid sequences.

21. (Previously presented) The polynucleotide according to claim 20, wherein said CD8  $\alpha$ -chain comprises all or a functional portion of a human CD8  $\alpha$ -chain.

22. (Previously presented) The polynucleotide according to claim 20 or 21, wherein said CD8  $\alpha$ -chain consists essentially of an extracellular domain of said CD8  $\alpha$ -chain and a transmembrane domain.

23. (Previously presented) The polynucleotide according to claim 22, wherein said transmembrane domain is a CD8  $\alpha$ -chain transmembrane domain.

24. (Canceled)

25. (Currently amended) The polynucleotide according to claim 20, wherein said therapeutic molecule of interest is selected from the group consisting of hemoglobin- $\beta$ , GATA-binding protein, d-aminoevulinate synthase, glucose-6-phosphate-dehydrogenase, Coagulation Factor VIII, Coagulation Factor XI, cystic fibrosis transmembrane conductance regulator, ornithine carbamoyl transferase,  $\alpha$ -L-iduronidase, iduronate-2-sulfatase,  ~~$\beta$ -hexosidase~~  $\beta$ -glucosidase,  $\alpha$ -galactosidase, galactosylceramidase, acid  $\alpha$ -glucosidase, hexamidase A, phenylalanine hydroxylase, collagen type IV,  $\alpha$ 5, Bloom Syndrome Gene Product, and low density lipoprotein receptor.

26. (Previously presented) An expression vector comprising the polynucleotide according to claim 20 or to claim 25.

27. (Previously presented) The expression vector according to claim 26, wherein said vector is selected from the group consisting of a recombinant adenovirus, a recombinant retrovirus, a recombinant adeno-associated virus, and a recombinant herpes virus.

28. (Previously presented) The expression vector according to claim 27, wherein said vector is replication defective.

29. (Currently amended) An expression vector according to claim 26 for expression in a target cell, wherein ~~said expression of said CD8  $\alpha$ -chain by said target cell~~ is designed to

inhibit[[s]] an immune response against vector-associated antigens, when expressed by said target cell.

30. (Currently amended) An expression vector according to claim 26 for expression in a target cell, wherein ~~said expression of said CD8  $\alpha$ -chain~~ is designed to inhibit[[s]] an immune response against said expression vector, when expressed.

31. (Previously presented) An improved viral expression vector having reduced immunogenicity comprising a non-viral nucleic acid consisting essentially of a nucleic acid sequence encoding a CD8  $\alpha$ -chain comprising a CD8  $\alpha$ -chain extracellular domain and a nucleic acid encoding for a therapeutic molecule of interest, wherein said CD8  $\alpha$ -chain is not a fusion protein.

32. (New) A composition comprising a target cell contacted by an expression vector encoding an immunomodulatory CD8 polypeptide including all or a functional portion of a CD8  $\alpha$ -chain resulting in expression of the CD8  $\alpha$ -chain on the surface of the target cell.

33. (New) The composition of claim 32 wherein the target cell includes a cell found in a tissue or an organ.

34. (New) The composition of claim 33 wherein the tissue or the organ includes one of a liver, a skin or an intestinal tract.

35. (New) The composition of claim 32 wherein the target cell can be present as a single entity, or can be part of a larger collection of cells.

36. (New) The composition of claim 35 wherein the larger collection of cells includes one of a cell culture, a tissue, an organ, or an organ system.

37. (New) The composition of claim 36 wherein the tissue includes an epithelial tissue.
38. (New) The composition of claim 35 wherein the organ includes one of a heart, a lung or a liver.
39. (New) The composition of claim 35 wherein the organ system includes a nervous system.
40. (New) The composition of claim 32 wherein the target cell, transplanted into the recipient, specifically inhibits an immune response in the host against vector-associated antigens.
41. (New) The composition of claim 32 wherein the CD8  $\alpha$ -chain includes a human CD8  $\alpha$ -chain.
42. (New) The composition of claim 32 wherein the CD8  $\alpha$ -chain includes a CD8  $\alpha$ -chain extracellular domain and a transmembrane domain.